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CAESAR, RIVISE, BERNSTEIN, COHEN & POKOTILOW, LTD. 11TH FLOOR, SEVEN PENN CENTER 1635 MARKET STREET PHILADELPHIA, PA 19103-2212			GOLLAMUDI, SHARMILA S	
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Please find below and/or attached an Office communication concerning this application or proceeding.

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DETAILED ACTION

Receipt for Continued Examination and Amendments filed July 1, 2005 is acknowledged.

Claims 48, 51-53, 58, 60-61, 64-67, 72, and 74 are pending in this application. Claims 1-47, 49-50, 54-57, 59, 62-63, 68-71, and 73 stand cancelled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 48, 51-53, 58, and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohno et al (5,958,453) in view of Gowan (5,876,759) in further view of Misra et al (5,869,098).

Ohno et al teach a solid pharmaceutical composition with improved disintegrability. The buccal dissolution time of the tablet is usually about 0.1-1.0 minutes, preferably about 0.1-0.8 minutes, more preferably about 0.1-0.5 minutes. See column 6, lines 63-68. Specifically the examples teach a dissolution time as fast as 23 seconds. The hardness of each tablet (measured

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with a tablet hardness tester) is usually about 2-15 kg, preferably about 3-10 kg. See column 6, line 63 to column 7, line 2. Ohno teaches the solid preparation which is capable of buccal disintegration or dissolution comprises (i) a pharmaceutically active ingredient, (ii) erythritol contained in a proportion of 5-90 parts by weight, (iii) crystalline cellulose and (iv) a disintegrant, preferably crospovidone contained in a proportion of 1-10 parts by weight. See column 2, lines 15-60. The solid pharmaceutical preparation further comprises mannitol of 150-mesh size (106 microns). The examples utilize 25% and 33% mannitol respectively. See column 5, lines 40-50 and examples. The solid pharmaceutical preparations comprises the pharmaceutical active agent in a proportion of 0.05-70% by weight, preferably about 0.1-50% by weight, more preferably 0.3-30% by weight. See column 4, lines 43-47. Ohno teaches various pharmaceutical actives that are suitable for the invention including instant aspirin and ibuprofen. See column 3, line 29. The composition can further include binders, acids, foaming agents, artificial sweeteners (aspartame), flavorants, lubricants, colorants, etc. See column 5, line 5 to column 6, line 15. Specifically the examples 3-4 utilize 1% magnesium stearate (lubricant). Table 7 teaches the use of 4% magnesium stearate and 1% light anhydrous silicic acid.

Firstly, Ohno et al do not teach a coated pharmaceutical agent. Secondly, although Ohno teaches the use of light anhydrous silicic acid (also known as silicon dioxide, colloidal silica, fumed silica, Cabosil, and Aerosil; see art of interest US 6,113,920), Ohno does not teach the instant precipitated silica.

Gowan teaches a compressed pharmaceutical dosage form containing pharmaceutical particles coated with a taste-masking composition, a water-disintegratable, compressible carbohydrate and a binder. The tablet disintegrates within 30 seconds after oral administration.

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See abstract. The compressed dosage form generally comprises from about 0.1% to about 45%, preferably about 12% to about 25%, of the coated pharmaceutical particle; from about 30% to about 90%, preferably about 40% to about 65%, of the water-disintegratable, compressible carbohydrate material to facilitate breakup (mannitol); from about 0.1% to about 5%, of the lubricant; from about 0.05% to about 5% of the sweetener; from about 0.05% to about 5%, of the flavor; and from about 0.01% to about 5% of the color. The example discloses a tablet containing coated acetaminophen (23%), mannitol (57%), microcrystalline cellulose (15%), aspartame, colloidal silicon dioxide (.06%), and stearic acid (.75%). Gowan teaches the particle size of the coated active and other components are generally less than 400 microns. Gowan teaches the use of a coating for the pharmaceutical active to provide taste-masking properties. See column 4, lines 35-50.

Misra teaches tablets that disintegrate rapidly when placed in the mouth. See abstract. Misra teaches the use of *conventional* tableting aids and additives include lubricants, glidants, anti-caking agents, and flow agents. Lubricants are used in amounts ranging from about 0% to about 10%, with about 0.01% to about 5.0% typically used. Glidants such as starch, talc, lactose, stearates, dibasic calcium phosphate, calcium silicate, Cabosil, Syloid 244 (instant precipitated silica), and silicon dioxide aerogels may be employed. Glidants are present in amounts ranging from about 0% to about 20%, with amounts of about 0.1% to about 5.0% being typical. See column 5, lines 15-40.

Firstly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings Ohno et al and Gowan and utilize a coated active in the composition. One would have been motivated to do so since Gowan teaches coating an

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active with a polymer to provide for taste-masking properties. Therefore, a skilled artisan would have been motivated to use a coated pharmaceutical in the composition of Ohno for its taste-masking property. Further, one could reasonably succeed by combining the references and since both references are directed to rapidly disintegrating dosage forms that dissolve in the oral cavity in less than 40 seconds.

Secondly, Ohno teaches the use of light silicic acid in the composition, which is an art recognized glidant and is also known as silicon dioxide, colloidal silica, fumed silica, Cabosil, and Aerosil (note art of interest 6,113,982). Thus, it would have been obvious for a skilled artisan to further look at Misra and substitute Ohno's glidant with the instant precipitated silica with the expectation of success. One would have been motivated to do so since Misra teaches that various silicas such as Syloid (a precipitated silica), Cabosil, and silicon dioxide aerogels are all used as glidants in the tableting art. Therefore, a skilled artisan would have reasonably expected similar results since the prior art recognizes the functional equivalency, i.e. they are used for the same purpose, of the instantly claimed silica and the prior art's silica. Thus, absent a showing of the criticality of the instant precipitated silica versus the prior art's functionally equivalent silica, it is considered *prima facie* obvious to substitute one art recognized equivalent for another art recognized equivalent.

With regard to the recitation of directly compressible polyol, the instant specification defines "compressible" polyols have a particle size of 100 to 500 microns; thus it is the examiner's position that Ohno's mannitol with a particle size of 150 mesh or 106 microns is considered a compressible polyol as defined by applicant on page 2 of the instant specification.

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With regard to claim 52, Ohno teaches 33% of mannitol in the composition and not instantly claimed 40-70%; however, this is deemed a manipulatable parameter wherein a skilled artisan would have been motivated to work within the general conditions of the prior art, to find the optimal range during routine experimentation. Moreover Gowan teaches the use of compressible sugars such as mannitol in the instant weight percent to facilitate breakup. Thus, one would have been motivated to increase the percent weight of the mannitol in Ohno to further facilitate breakup of the tablet after oral administration. Generally difference in concentrations do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such as concentration is critical. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 48, 51-53, 58, 60-61, 64-67, 72, and 74 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 7, and 11-12 of U.S. Patent No. 6,106,861 in view of Ku et al (5,994,348). Although the conflicting claims are not identical, they are not patentably distinct from each other

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because the claimed subject matter in instant application and US patent '861 are obvious modifications of each other.

US patent claims a multiparticulate tablet, which disintegrates in the mouth in less than 40 seconds, comprising A) particles of coated active principle and B) mixture of excipients of 3-15% of a disintegrant selected from crosslinked PVP or crosslinked sodium carboxymethylcellulose, and 40-90% of at least one soluble diluent with binding properties, said polyol being directly compressible form with a diameter of 100-500 micrometers or a powder form with a diameter of less than 100 micrometers wherein the polyol with less than 13 carbon atoms selected from mannitol xylitol, sorbitol, and maltitol; wherein when the composition contains at least two soluble diluent agents, one part of which is a directly compressible form while the other part is in powder form, the proportion of directly compressible polyol to powder polyol being from 99/1 to 50/50. Dependent claims recite aspirin, ibuprofen, ketoprofen, loperamide, and paracetamol.

Instant application recites a multiparticulate tablet, which disintegrates in contact with the saliva in the mouth in less than 40 seconds comprising A) particles of coated active principle, and B) mixture of excipients being free of effervescent agents and the ratio of excipient mixture to coated active principle particles being 0.4 to 6 parts by weight, the mixture of excipients comprising: a disintegration agent; 30-90% of a soluble diluent with binding properties which is a directly compressible polyol selected from mannitol, xylitol, and maltitol, with an average particle diameter of 100 to 500 um, 0.05-2% lubricant, the proportion of disintegration agent being 1 to 15% by weight, at least one flavor, sweetener, or color; and 0.1-

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10% of a permeabilizing agent selected from precipitated silicas, maltodextrins, and beta-cyclodextrins.

Independent claim 61 is directed a multiparticulate tablet, which disintegrates in contact with the saliva in the mouth in less than 40 seconds comprising A) particles of coated active principle, and B) mixture of excipients being free of effervescent agents and the ratio of excipient mixture to coated active principle particles being 0.4 to 6 parts by weight, the mixture of excipients comprising: a disintegration agent; 30-90% of at least two soluble diluents with binding properties which consists of a polyol selected from mannitol xylitol, and maltitol and at least one diluent is a directly compressible polyol with an average particle diameter of 100 to 500 micrometers and at least one diluent agent is a powder form with a diameter of less than 100 micrometers wherein the ratio of compressible polyol to powder polyol is 99/1 to 20/80; 0.05-2% lubricant, the proportion of disintegration agent being 1 to 15% by weight, at least one flavor, sweetener, or color; and 0.1-10% of a permeabilizing agent selected from precipitated silicas, maltodextrins, and beta-cyclodextrins.

Ku et al teach a pharmaceutical composition with excellent wetting, disintegration, and rapid release properties (col. 2, lines 5-15). Ku teaches the use of one or more disintegrants, which are capable of facilitating the break up of a tablet when placed in contact with an aqueous medium. Among the disintegrants that meet this criteria, croscarmellose is taught in a range of 2-5%. See column 3, line 65 to column 4, lines 20. Ku teaches the use of anti-adherents such as silicon containing compounds in the amount of .25-5% reduce the stickiness of the formulation and prevent adherence to metal surfaces. (col. 4, lines 20-30). Particularly Syloid 244, which is a precipitated silica is exemplified. Further, Ku teaches the combination of magnesium stearate

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and silicon dioxide provides a superior lubrication effect while minimizing any decline in tablet dissolution performance (col. 5, lines 59-65).

Firstly, it is noted that US '861 is directed to overlapping subject matter wherein both US '861 and the instant claims recite the critical components of a) a coated pharmaceutical, b) a disintegrating agent, and c) a compressible polyol selected from mannitol xylitol, and maltitol with overlapping weight percents. Further, US '861 recited open-ended claim language, i.e. comprising, which can include other additives such as instant permeabilizing agent and lubricants. Therefore, it would have been obvious for one of ordinary skill in the art at the time the invention was made to look to the teachings of Ku et al and include conventional additives such as precipitated silica and a lubricant such as magnesium stearate in the composition of US '861 and arrive at instantly claimed invention. One would have been motivated to do so since Ku teaches the advantages of using a magnesium stearate and Syloid 244 provides a superior lubrication effect to reduce stickiness of the composition to metal surfaces during the process of making the dosage forms, while minimizing any decline in tablet dissolution performance.

Claims 48, 51-53, 58, 60-61, 64-67, 72, and 74 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over copending Application No. 09/914544 (claims 21, 24-26, 28-29, 36) and 10/494505 (claims 1-9). Although the conflicting claims are not identical, they are not patentably distinct from each other because all the applications are directed to similar subject matter.

Instant application recites a multiparticulate tablet, which disintegrates in contact with the saliva in the mouth in less than 40 seconds comprising A) particles of coated active principle, and B) mixture of excipients being free of effervescent agents and the ratio of

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excipient mixture to coated active principle particles being 0.4 to 6 parts by weight, the mixture of excipients comprising: a disintegration agent; 30-90% of a soluble diluent with binding properties which is a directly compressible polyol selected from mannitol, xylitol, and maltitol, with an average particle diameter of 100 to 500 um, 0.05-2% lubricant, the proportion of disintegration agent being 1 to 15% by weight, at least one flavor, sweetener, or color; and 0.1-10% of a permeabilizing agent selected from precipitated silicas, maltodextrins, and beta-cyclodextrins.

Independent claim 61 is directed a multiparticulate tablet, which disintegrates in contact with the saliva in the mouth in less than 40 seconds comprising A) particles of coated active principle, and B) mixture of excipients being free of effervescent agents and the ratio of excipient mixture to coated active principle particles being 0.4 to 6 parts by weight, the mixture of excipients comprising: a disintegration agent; 30-90% of at least two soluble diluents with binding properties which consists of a polyol selected from mannitol xylitol, and maltitol and at least one diluent is a directly compressible polyol with an average particle diameter of 100 to 500 micrometers and at lest one diluent agent is a powder form with a diameter of less than 100 micrometers wherein the ratio of compressible polyol to powder polyol is 99/1 to 20/80;, 0.05-2% lubricant, the proportion of disintegration agent being 1 to 15% by weight, at least one flavor, sweetener, or color; and 0.1-10% of a permeabilizing agent selected from precipitated silicas, maltodextrins, and beta-cyclodextrins.

Copending application '544 is directed to: A rapidly disintegrating tablet similar to those designed to disintegrate in the mouth on contact with saliva in less than 30 seconds, forming an easy- to-swallow suspension, obtained by direct compression of a dry mixture of coated

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microcrystals or microgranules of an active substance and excipients including at least one disintegrating agent, a soluble agent and a lubricating agent, wherein the lubricating agent is in powder form its friability is less than 1 %, whereby said tablet can be packaged by standard process and has the required and adequate hardness to enable it to be removed with ease from the blister pack in which it is packed, by perforating the seal thereof by pushing the tablets with a substantially reduced risk of the tablet breaking during removal. Depending claims 24-25 are directed to a lubricant (instant magnesium stearate) and dependent claim 28 is directed to instant crospovidone or croscarmellose as the disintegrant. Dependent claim 29 is directed to a mixture of excipients including a permeabilizing agent, a solubilizing agent, sweeteners, and flavors. Firstly, it should be noted that the claim is directed to a product and the product-by-process limitations are not given patentable weight. See MPEP section 2113, “even though product by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production, if the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior art was made by a different process.” *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.Cir. 1985). Secondly, it should be noted that the limitations of ‘544 after the “whereby” clause is intended use and is not given patentable weight.

The instant application and copending application ‘544 are directed to similar and overlapping subject matter that claims the critical elements of (1) a tablet that disintegrates wherein the instant “in less than 40 second” encompasses copending’s “less than 30 seconds”; (2) a soluble agent wherein ‘544’s is directed to the generic soluble agent and the instant

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application is directed to the species “mannitol, maltitol, and xylitol.”; (3) a disintegrating agent selected from crospovidone or croscarmellose wherein the instant claims are directed to the species and copending’s independent claim is directed to the genus (however dependent claims are directed to the same disintegrant); (4) a coated active agent. Further ‘544 can further include a permeabilizing agent. Thus, the instant and copending application are obvious over each other.

Copending ‘505 is directed to a fast release tablet which disintegrates in the mouth upon contact with saliva in less than 40 seconds, preferably in less than 30 seconds, comprising at least one active substance in the form of coated microcrystals or microgranules and on a mixture of excipients in the form of grains comprising: from 60 to 85% of a diluent, from 3% to 20% of a disintegrant, from 1% to 8% of a sweetener, from 0% to 5% of a flow agent, from 0% to 10% of a binder, from 0% to 10% of a permeabilizing agent, swelling agent and/or lubricant, and in that the grains of excipients have a median particle size of between +30 and -30%, preferably between +10 and -10%, relative to the size of the coated microcrystals or microgranules.

Dependent claims 2 is recites instant diluent (polyols wit less than 13 carbons, particularly mannitol, xylitol, maltitol) in a Markush group and the instant disintegrant (crospovidone croscarmellose) in a Markush group.

The instant application and copending application ‘505 are directed to similar and overlapping subject matter that claims the critical elements of (1) a tablet that disintegrates wherein the instant “in less than 40 second”; (2) a soluble agent wherein ‘505’s independent claim is directed to the generic soluble agent and dependent claim 2 recites the instantly claimed diluent (mannitol, maltitol, and xylitol); (3) a disintegrating agent wherein ‘505’s independent claim is directed to the generic disintegrating agent and dependent claim 2 recites the instantly

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claimed disintegrant (crospovidone and croscarmellose); (4) a coated active agent; (5) a permeabilizing agent; and (6) a lubricant. Thus, the instant and copending application are obvious over each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claims 48, 51-53, 58, and 60 are rejected. Claims 61, 64-67, 72, and 74 are free of prior art but are rejected under obviousness double patenting.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Sharmila S. Gollamudi
Examiner
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